Oral Testimony Before the CASAC Ozone Review Panel on the Third Draft Ozone ISA

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Thank you for the opportunity to speak today on behalf of the American Petroleum Institute. These comments will focus on the plausibility of a causal association between adverse respiratory and cardiovascular effects and short-term and long-term ozone exposures below the current standard, based on evidence presented in the third draft ISA (US EPA, 2012).

For short-term respiratory effects the evidence from controlled experimental and observational studies does not support an adverse response below the current standard. EPA cites evidence from human controlled exposure studies, but these indicate that effects are neither statistically significant nor adverse at levels below the current standard. Similarly, evidence from animal studies report mild ozone effects in the range of 100-200 ppb that are not informative for exposures below the current standard, and the single study reporting airway hyper-responsiveness in 3 of 9 rat species after 50 ppb ozone exposures for 8 hours is not sufficient evidence of adverse effects at low ozone levels.

Recent epidemiology studies that examined associations between short-term ambient ozone exposure and respiratory morbidity have reported mixed results across different health endpoints. Many of the studies on which EPA relied for its causality determination had numerous limitations and uncertainties that were not fully considered. These include confounding by other pollutants, use of central monitors, the unreliability of peak expiratory flow rate measurements, and the biological implausibility of lag times for effects on pulmonary function. EPA should more robustly explain these limitations and uncertainties.

For example, one of the key epidemiology studies, the study by Mortimer *et al*. (2002), used subject-administered lung function measurements, reported no significant effects for ozone in multi-pollutant models, and reported positive findings only at biologically implausible lag times. In fact, EPA noted in the 2008 nitrogen dioxide ISA that the same study was unreliable because of its use of self-administered data. Many studies confirm that self-administered peak expiratory flow measurements are too unreliable to make definite conclusions on the health effects of criteria pollutants. In another example, EPA noted that the results of the study by O'Connor *et al.* (2008) supported its conclusion that current levels of ozone caused lung function decrements in asthmatic children. EPA did not consider, however, that the results were not statistically significant and that the magnitude of the response for ozone was small compared to that reported from other pollutants. The same study also reported no associations between ozone and asthma symptoms or school absences. These are only two examples of many similar uncertainties and inconsistencies that need to be weighed and considered more fully in making causality determinations for adverse effects below the current level of the ozone standard.

Cardiovascular effects associated with short-term ozone exposures are even more uncertain. EPA has acknowledged this uncertainty and concluded that evidence is only suggestive of a causal relationship because of the lack of coherence within the science and weak biological plausibility. The suggestive

evidence is primarily from animal studies that have shown effects at levels well above the current ozone standard.

For mortality from acute ozone exposures, EPA has relied exclusively on multi-city epidemiology studies that have reported relatively small, but significant, pooled estimates of all-cause mortality. The findings from these studies are difficult to interpret because of the many unresolved and unexplained sources of bias and the inconsistencies in results across studies, even for those using similar datasets and modeling assumptions. The heterogeneity in ozone-mortality effect estimates across cities remains unexplained. There is also little ozone mortality evidence from animal studies; only pre-morbidity markers of disease have been linked with plausible mortality effects, and these are dubious.

Lastly, the evidence for adverse health effects from long-term exposures to ozone is even less. EPA upgraded its evidence classification to a "likely to be causal relationship" based on reported associations of new-onset asthma with specific gene variants. These studies are too few for confidence in the findings and do not add appreciably to the prior evidence that EPA deemed to be suggestive. The more robust toxicology evidence is still too uncertain because of issues associated with extrapolating data from compromised animal models to humans, from high-exposure regimens to more typical ambient exposures, and because of inconsistencies across studies.

Evidence of mortality associated with long-term ozone exposures is the weakest of all, as recognized in CASAC member comments on previous ISA drafts. Only two new studies were available since the last ozone review and they offered conflicting evidence. EPA should rely on prior analyses of long-term ozone exposures and mortality, which highlight the lack of consistently positive associations among several large cohort studies, including the Harvard Six Cities study (Dockery *et al*., 1993), the American Cancer Society study (Pope *et al*., 2002), the US Veterans' Cohort study (Lipfert *et al*., 2000), and the Adventist Health Study of Smog (Abbey *et al*., 1999).

In conclusion, the overall body of new evidence presented in the third draft ozone ISA does not support adverse health effects at levels below the current ozone standard. EPA should reconsider its causality determinations, and fully explain how the consistency, coherence, and limitations of each new piece of information was weighed in the causality conclusions.

References

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